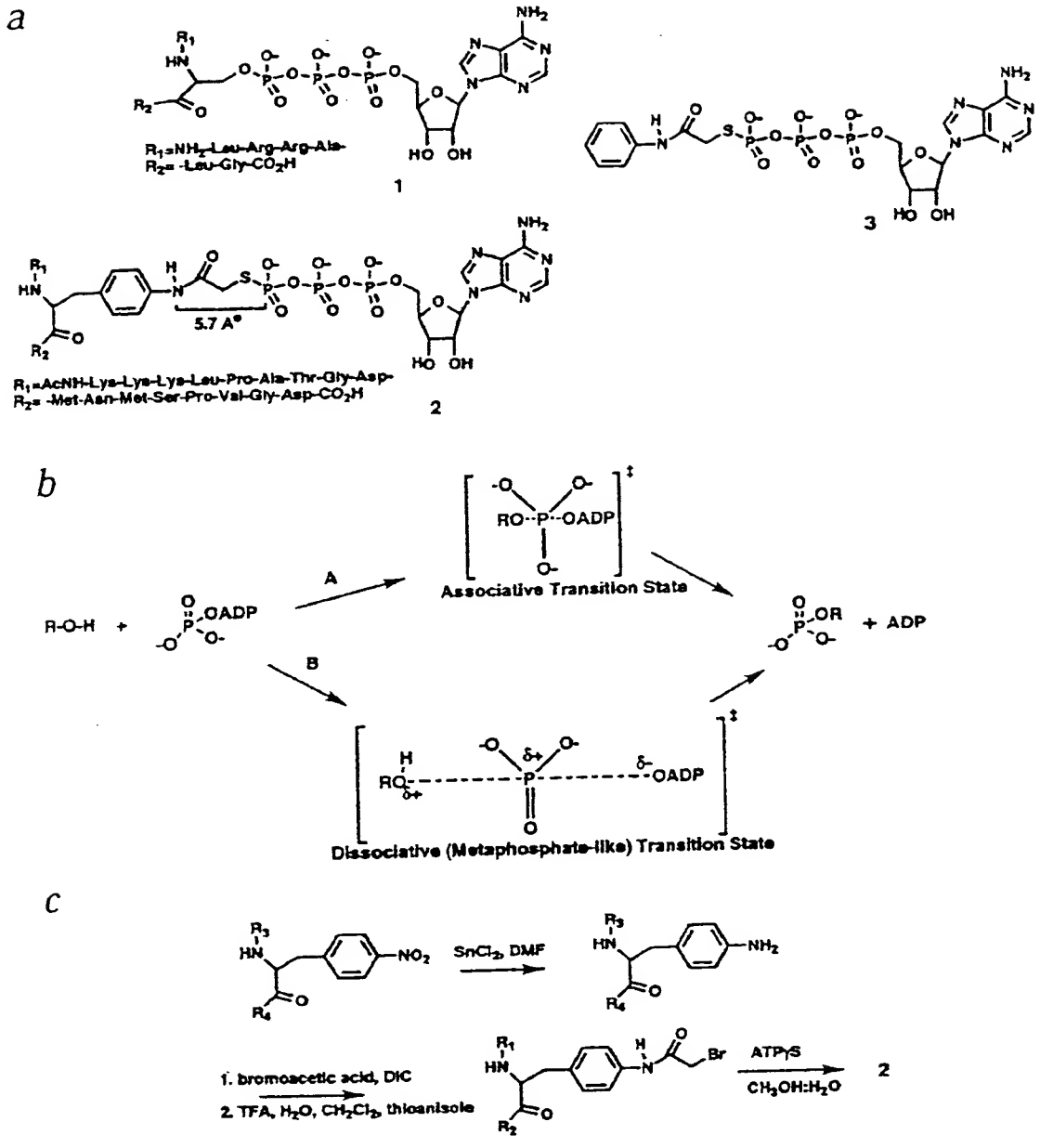
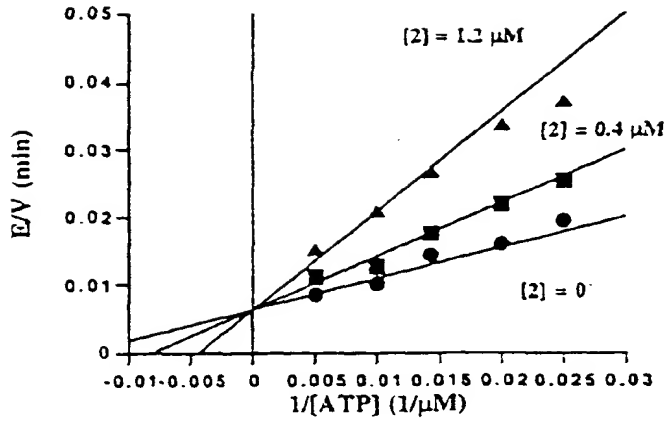
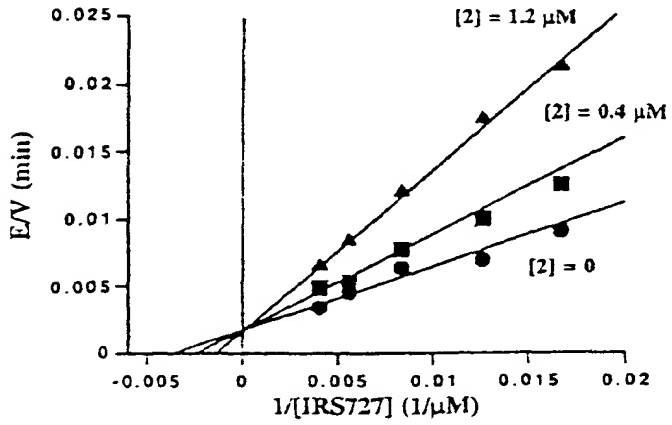

a
R1=NH2-Leu-Arg-Arg-Ala-
R2= -Leu-Gly-CO2H
1
3
5.7 A°
R1=AcNH-Lys-Lys-Lys-Leu-Pro-Ala-Thr-Gly-Asp-
R2= -Met-Asn-Met-Ser-Pro-Val-Gly-Asp-CO2H
2
b
R-O-H
OADP
A
B
Associative Transition State
Dissociative (Metaphosphate-like) Transition State
+ ADP
c
SnCl2, DMF
1. bromoacetic acid, DIC
2. TFA, H2O, CH2Cl2, thioanisole
ATPγS
CH3OH:H2O
2

FIG. 1

a


0.05
0.04
0.03
0.02
0.01
0
E/V (min)
[2] = 1.2 μM
[2] = 0.4 μM
[2] = 0
-0.01 -0.005 0 0.005 0.01 0.015 0.02 0.025 0.03
1/[ATP] (1/μM)

b


0.025
0.02
0.015
0.01
0.005
0
E/V (min)
[2] = 1.2 μM
[2] = 0.4 μM
[2] = 0
-0.005 0 0.005 0.01 0.015 0.02
1/[IRS727] (1/μM)

c

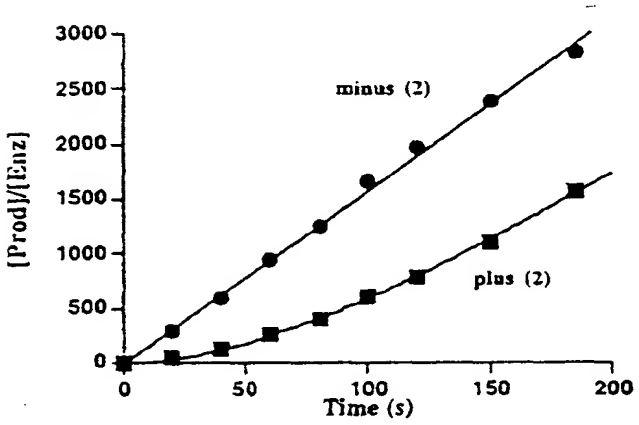

3000
2500
2000
1500
1000
500
0
[Prod]/[Enz]
minus (2)
plus (2)
0 50 100 150 200
Time (s)

FIG. 2

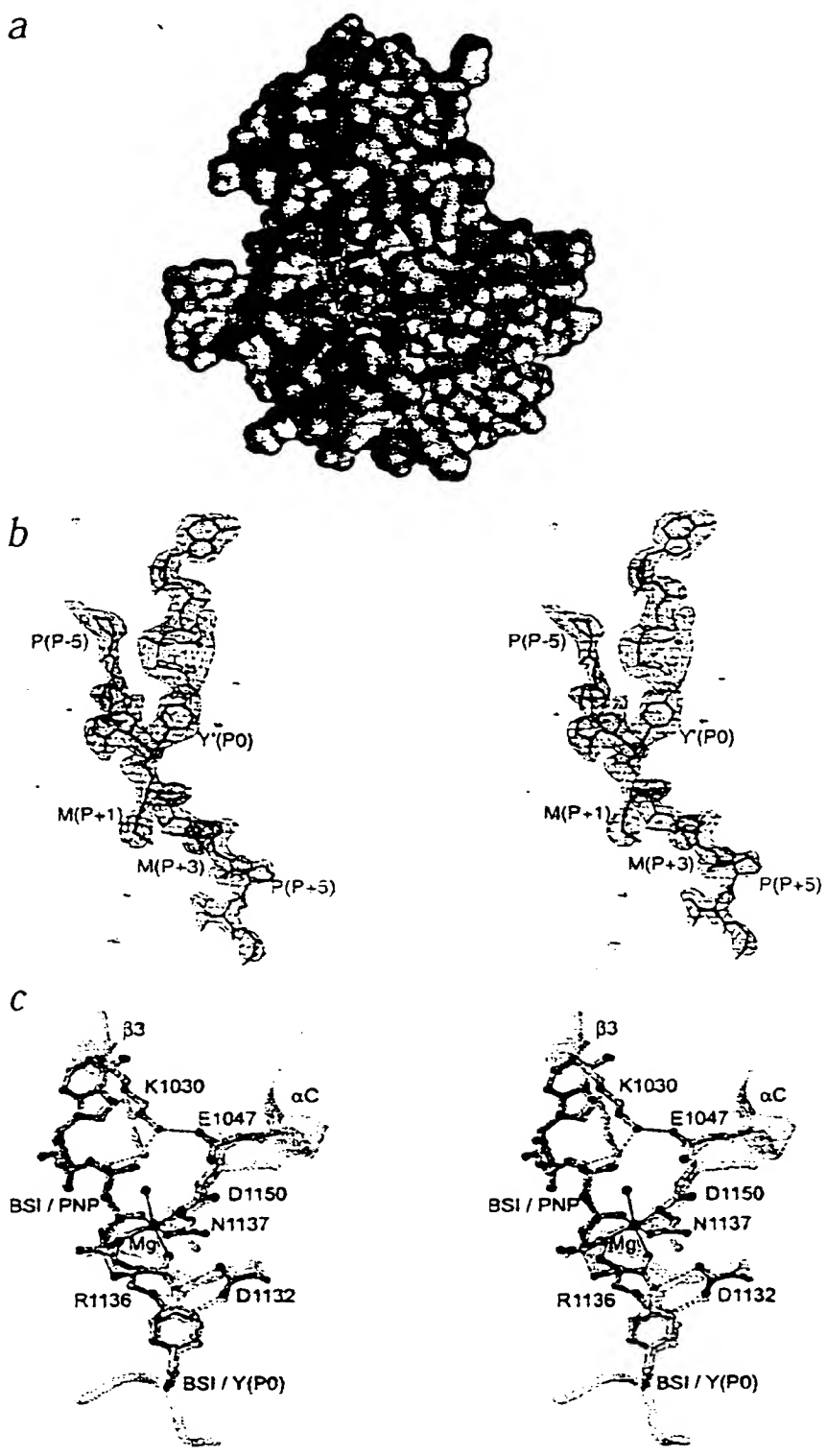
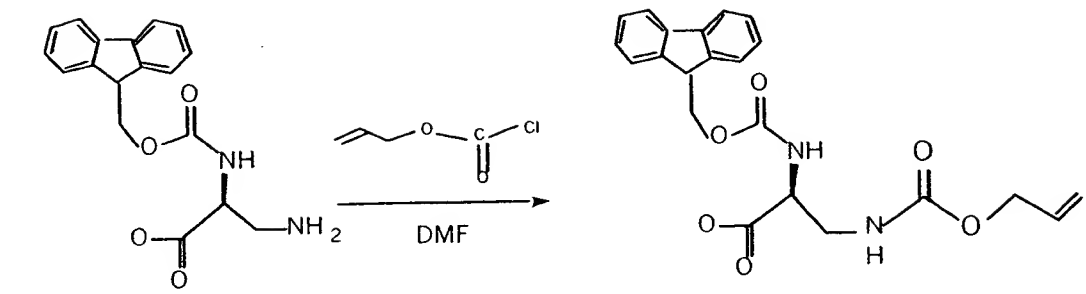
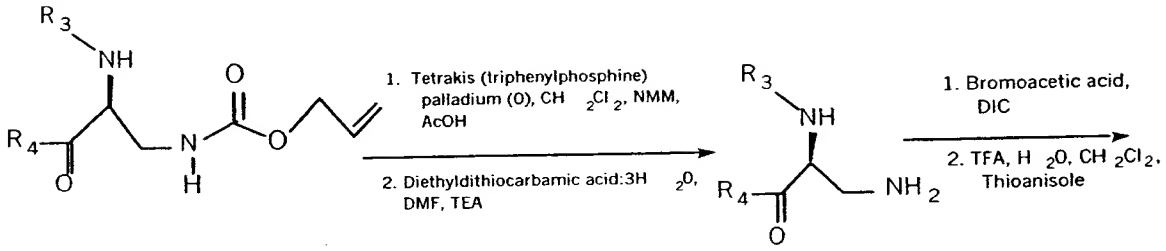
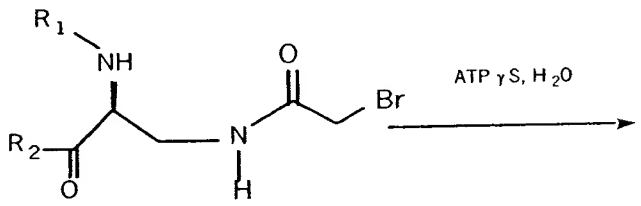
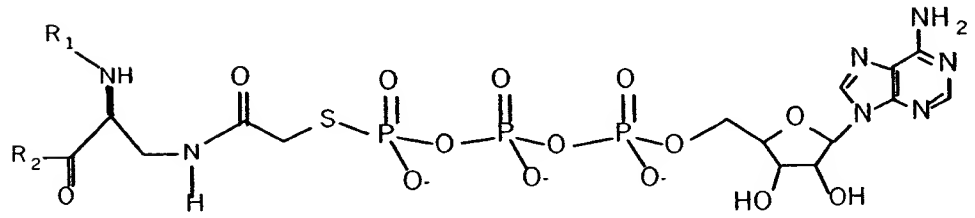

a
b
P(P-5)
Y'(P0)
M(P+1)
M(P+3)
P(P+5)
P(P-5)
Y'(P0)
M(P+1)
M(P+3)
P(P+5)
c
β3
K1030
αC
E1047
D1150
BSI / PNP
N1137
Mg
R1136
D1132
BSI / Y(P0)
β3
K1030
αC
E1047
D1150
BSI / PNP
N1137
Mg
R1136
D1132
BSI / Y(P0)

FIG. 3





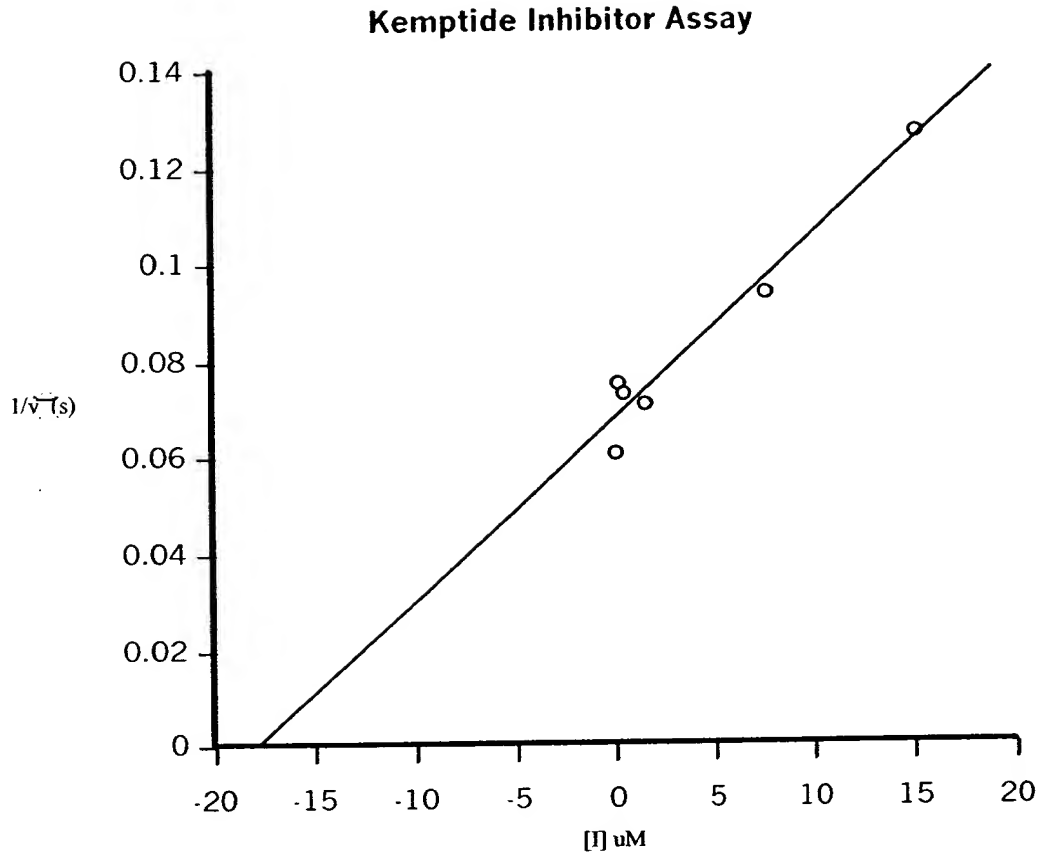




Compound 4

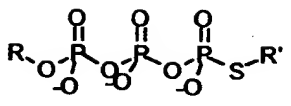
R_1 = AcNH-Leu-Arg-Arg- Ala-
R_2= -Leu-Gly-COOH
R_3= R_1 with Arg protecting groups
R_4= R_2 with Gly linked to Wang resin

FIG. 4



Inhibition assay for protein kinase A.
Final concentrations for reaction components : ATP = 15 uM,
kemptide = 25 uM, Mg2+ = 10mM, Tris-HCl = 40 mM,
bovine serum albumin (from enzyme mix) 150 ug/mL.
All reactions were carried out at pH 7.5 and with a
final enzyme concentration of 0.35 nM
for 2 minutes at 30 degrees Celsius.

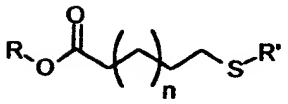
FIG. 5



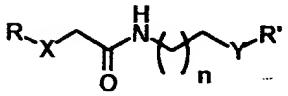
R'=CH2CO-peptide or peptidomimetic

R=adenosine or nucleoside analog

n=0-6

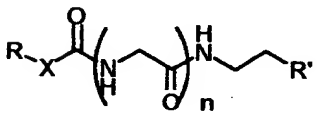


n=0-6

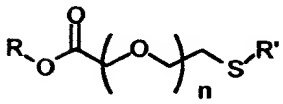


n=0-6

X=O, NH, S, CH_2
Y=O, NH, S, CH_2



X=O, NH, S, CH_2 n=0-6



n=0-6